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(12) **United States Patent**  
**Ajami**(10) **Patent No.:** **US 6,284,219 B1**  
(45) **Date of Patent:** **\*Sep. 4, 2001**(54) **IN VIVO DETERMINATION OF METABOLIC  
FUNCTION FOR USE IN THERAPY  
MANAGEMENT**(75) Inventor: **Alfred M. Ajami**, Brookline, MA (US)(73) Assignee: **Phenome Sciences Inc.**, Woburn, MA  
(US)

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424/1.65, 1.81, 9.2; 435/4, 183, 188, 814;  
250/472.1; 600/9(56) **References Cited****U.S. PATENT DOCUMENTS**

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*Primary Examiner*—José G. Dees*Assistant Examiner*—Dameron L. Jones(74) *Attorney, Agent, or Firm*—Weingarten, Schurgin, Gagnebin & Hayes LLP(57) **ABSTRACT**

It is an object of the present invention to provide in vivo analytical methods that allow for diagnosis and management of therapy for diseases involving discrete biochemical pathways. In the method of the invention, a labelled tracer probe, a specifically designed substrate of a "gateway" enzyme, an enzyme marking a regulatory point in a discrete biochemical pathway, is administered to a subject; a labelled product of the action of the enzyme is measured; and the appearance and concentration of the product are related to the disease condition of interest. Determination of the rate of substrate-product conversion of the gateway enzyme allows for the analysis to be made. The method involves administering a defined amount of a labelled "metaprobe" substrate of the gateway enzyme to a subject, at a site that provides access to a desired pool of the gateway enzyme in the subject, and measuring the amount of the chosen labelled product. The presence and amount of the chosen labelled product in, e.g., the breath, definitively indicates that the labelled metaprobe has been metabolized by the specific enzyme in the specific biochemical pathway under consideration, and from the calculated rate of substrate-product conversion by the gateway enzyme, the desired diagnostic determination may be made.

**31 Claims, 15 Drawing Sheets-**